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Echinacea purpurea root extract modulates diabetes-induced renal dysfunction in rats through hypoglycemic, antioxidants, and anti-inflammatory activities

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ABSTRACT

Introduction: Diabetes (DIAB)-related renal dysfunction is one of the most severe complications of the condition, which comes to an end with chronic renal failure. *Aim:* This study aimed to examine if *Echinacea purpurea* (*E. purpurea*) root extract could help protect kidneys from damage caused by DIAB in rats. *Methods:* DIAB was induced in four experimental rats groups (n = 10) by injecting STZ (65 mg/kg). One of the DIAB groups was left untreated, and the other three groups were treated with either *E. purpurea* root extract alone (200 mg/kg), metformin (Met) alone (200 mg/kg), or both together. A group of healthy rats (control) was also used for comparison. *Results:* In contrast to the DIAB group, *E. Purpurea* root extract alone and combined to Met improved body weight, kidney index, kidney function (creatinine and urea), and renal pathology. Compared to the DIAB group, the ingestion of *E. purpurea* extract alone or in combination with Met reduced blood glucose levels, bringing them back into the normal range in the combination group and ameliorating hemoglobin A1c(HbA1c) levels. The extract group's antioxidant effect was clearly demonstrated by the decreased malondialdehyde (MDA) and increased superoxide dismutase (SOD) kidney concentrations in the extract group alone or in combination with Met where the combination showed superior activity. The extract group's anti-inflammatory effect was observed from the reduced serum levels of interleukin 1β (IL-1β) and IL-6 in the extract group alone or mixed with Met, where the mixture showed a better action. *Conclusion:* In rats, *E. purpurea* root extract ameliorated DIAB-related nephrotoxicity induced by STZ. The hypoglycemic, antioxidant, and anti-inflammatory properties of the extract may be the underlying mechanisms.

Keywords: Diabetes, nephrotoxicity, *Echinacea purpurea*, antioxidants, anti-inflammatory, histopathology.

1. INTRODUCTİON

Diabetes (DIAB) is becoming more common all over the world. In Saudi Arabia, it was recently estimated that 30% of the population is diabetic (Alharbi and Alhazmi, 2020). It is a complex disease that causes significant health problems. It harms patients' quality of life *via* inflammation and oxidative stress, which are responsible for DIAB complications such as vascular disorders and kidney failure(Ahangarpour et al., 2009; Akpaso et al., 2011; Chien-Feng et al., 2018). Diabetic patients are more susceptible to diabetic nephropathy (DN) (20-50% of diabetic patients progress DN). Renal injury secondary to DIAB is the most common cause of renal failure (Dallak et al., 2018). Chronic hyperglycemia-induced glucose autooxidation, stimulating inflammatory biomarkers, and the generation of reactive oxygen species (ROS). This represents a common mechanism underlying vascular injury perceived in insulin resistance and is highly correlated to DIAB's progression (Shoelson et al., 2006; Forbes et al., 2008; Lewko and Stepinski, 2009). Additionally, hyperglycemia-induced oxidative insult in renal tubular epithelial cells initiates tubular fibrosis and kidney failure (Morcos et al., 2002; Lin et al., 2005).

Slowing down DN progression and controling of DN in the early stage for prevention of end-stage renal disease and renal failure occurrence is of utmost importance to several researchers. Medical plants with antioxidant and anti-inflammatory properties present an opportunity for integrative therapy for DN. Antioxidant and anti-inflammatory agents have vital roles in preventing hyperglycemia-induced DN and its health benefits that protect from DN's progression and prevent renal failure (Marotta et al., 2010). *Echinacea purpurea* (*E. purpurea*), purple coneflower, contains many active compounds as flavonoids, polysaccharides, total polyphenols, alkylamides, and isobutylamides (Barnes et al., 2005). The extract of *E. purpurea* root has a wide spectrum of pharmacological properties (Esfanjani et al., 2018). It exhibited anticancer (Tsai et al., 2012), antioxidant (Oniszczuk et al., 2016), immunostimulant (Barnes et al., 2011), anti-inflammatory (Ol´ah et al., 2017), antibacterial (Chiellini et al., 2017), and antiviral (Turner et al., 2000) properties.

Previously, it has been revealed that the active compounds of *E. purpurea* improved insulin sensitivity (Kotowska et al., 2014). The efficiency of aqueous extract of herbs mixture including *E. purpurea* root in diabetic rabbits revealed the hypoglycemic and hypolipidemic effects, with restored liver and muscle glycogen levels (Aghajanyan and Trchounian, 2018). Nano-*E. purpurea* improved hyperglycemia and insulin resistance. It also has a significant effect in modulating reproductive dysfunction and reducing the reactive oxygen species (ROS) concentrations in streptozotocin (STZ) diabetic rats (Chien-Feng et al., 2018). As far as we know, there is no previous research comparing the effect of *E. Purpurea* root extract, metformin (Met), and their mixture in attenuating DN. The study also examined the nephroprotective mechanisms of *E. purpurea* extract focussed on oxidative stress and inflammation.

2. METHODOLOGY

Drugs and chemicals

Metformin (Met)as tablets containing 500 mg metformin hydrochloride (Merck Serono, Middle East) obtained from KAU Hospital, Jeddah, Saudi Arabia. STZ was obtained from Thermo Fisher (Kandel) (GmbH, Karlsruhe, Germany).

Kits

Enzymatic colorimetric kits were purchased from Centronic Chem. Co, Germany.Enzyme-linked immunosorbent assay ELISA kits were obtained from Bioassay Technology Laboratory, Shanghai, China.

***E. Purpurea* root extract**

E. Purpurea root in a liquid extract (97% *E. Purpurea* root extract) was purchased from iHerb. Com, HERB PHARM, Saudi Arabia, Country of origin of goods (USDA ORGANIC) (each 1 ml equals about 300 mg of dried herb of *E. Purpurea* root). It contains essential oil, alkamides, alkaloids, caffeic acid derivatives, flavonoids, anthocyanins, phenolic acids, polysaccharides, and glycoproteins.

Animals

Fifty adult male Albino rats (200–240 g) were obtained from the animal house, King Fahd Medical Research Center, KAU. Before the experiment, all animals were given a week of acclimatization in normal laboratory conditions. Rats were served a well-balanced diet and had access to unlimited water. The animal handling and procedures were conducted following Canadian regulations. The experimental study was conducted from May 2020 to March 2021.

Ethical approval

This work was approved by the biomedical ethics research committee, The Deanship of Scientific Research, King Abdul-Aziz University KAU, ethical approval (Reference No (172060354). All procedures performed in the experimental study were in accordance with the ethical standards.

Induction of DIAB

Rats were given STZ (65 mg/kg) intraperitoneally (i.p.) after fasting for 12 hours. STZ was prepared immediately before use by dissolving in sodium citrate buffer (10 mM, pH 4.5) (Bennett and Pegg, 1981). Rats were supplied with sucrose solution (5%) for 48 h after STZ injection (Peschke et al., 2000). After 72 h, A glucometer (Roche One Touch® Ultra, Lifescan, Johnson & Johnson, Milpitas, CA) was used to estimate fasting blood glucose (FBG) in the blood samples withdrawn from the tail vein. Only rats with FBG ≥ 250 mg/dl were considered diabetic (Damasceno et al., 2012).

Experimental protocol

Male rats (n=50) were divided into 5 groups (10/group) as follows: 1- Control, rats injected with a single i.p. dose of the citrate buffered; 2- Diabetic; 3- Diabetic + *E. purpurea*, diabetic rats received *E. Purpurea* (200 mg/kg) (Ramasahayam et al., 2011); 4- Diabetic + Met, diabetic rats received Met (200 mg/kg) (Ellen et al., 2018); 5- Diabetic + *E. purpurea* + Met, diabetic rats received *E. purpurea* and Met. The study was continued for 8 weeks to meet the renal complications (Knoll et al., 2005).

Body weights were weekly recorded throughout the experiment (8 weeks) to monitor weight changes and adjust *E. purpurea* and Met doses. The body weight gain percentage (BWG%) was estimated. After completion of the experiment, the rats were anesthetized, blood samples were collected, and serum samples were separated and stores at -80°C until used for biochemical measurments. Kidney weight was recorded, and the kidney index for all rats was calcaulated by dividing the total weight of the left and right renal by the rat's weight (Erdem et al., 2000). The left renal samples were fixed in 10 % formaldehyde for subsequent histopathological evaluation. The right renal samples were kept frozen at -80°C for biochemical analysis.

Determination ofserum glucose and glycated hemoglobin (HbA1c)

The serum concentration of glucose was assessed by the enzymatic colorimetric kit. The serum HbA1c was determined by ELISA kit as described in manufacture procedures.

Determination of serum kidney functions

Serum concentrations of creatinine and blood urea nitrogen were determined using the enzymatic colorimetric kits following the manufacturing procedures.

Determination of pro-inflammatorycytokines indices

Serum concentrations of interleukin 1β (IL-1β) and IL-6 were determined by double-antibody sandwich enzyme-linked immunosorbent assay ELISA kits.

Determination of kidney oxidative stress indices

The homogenized kidney samples were used to measure the activity of superoxide dismutase (SOD) and the content of malondialdehyde (MDA) by double-antibody sandwich enzyme-linked immunosorbent assay ELISA kits.

Histopathological examination

After the routine procedure and hematoxylin and eosin (H & E) staining, the kidney tissues were examined under a light microscope by a blind histopathologist for any pathological change.

Statistical analysis

All data were represented as mean ± SD,and means were compared by ANOVA (P-value of≤ 0.05 was considered significant) using SPSS version 25 for windows.

3. RESULTS

Impact of *E. purpurea*, Met and their mixture on some biological variables evaluated in the diabetic rats

The rats' initial body weights (IBW) were identical in all groups at the start of the experiment. After 8 weeks, diabetic rats revealed a significant bodyweight loss which was confirmed by a significant decline in final body weight (FBW) and BWG% relative to the control rats ($p \leq 0.001$). Administration of *E. purpurea,* Met, and their mixture to diabetic rats revealed a significant ($p \leq 0.001$) improvement in both FBW and BWG% compared to the diabetic group. Furthermore, diabetic rats treated with Met alone and Met plus *E. purpurea* generated a significant increase in FBW and BWG% ($p \leq 0.001$) relative to their corresponding values in the *E. purpurea* treated diabetic rats. There was no significant difference between diabetic rats treated with either Met or *E. purpurea*+ Metconcerning FBW and BWG% (Table 1).

Table 1 Impact of *E. purpurea*, Met and their mixture on FBW and BWG % evaluated in the diabetic rats.

Groups	IBW (g)	FBW (g)	BWG (%)
Control	227.2 ±9.62	306.4 ± 19.06	34.9± 4.04
Diabetic	223.8 ± 8.36	192.2 ± 12.87[a]	-14.1 ± 5.32[a]
Diabetic+ *E. purpurea*	229.1 ± 5.72	243.0 ± 21.78[b]	6.2 ± 2.31[b]
Diabetic+Met	228.1 ± 8.65	281.7 ± 13.80[b,c]	23.5± 4.26 [b,c]
Diabetic+ *E. purpurea* +Met	230.8 ± 6.96	291.1 ± 12.36[b,c]	26.1± 4.28 [b,c]

Values are presented as mean ± SD (n=10). Significant difference relative to [a]Control; [b]Diabetic; and [c]Diabetic+ *E. purpurea*.
FBW: Final body weight; BWG%: Body weight gain %.

Concerning kidney weight and kidney index, diabetic rats had a significantly higher kidney weight and kidney index than control rats($p \leq 0.001$). In diabetic rats, *E. purpurea*, Met, and their mixture resulted in a substantial reduction in kidney weight and kidney index relative to the diabetic rats($p \leq 0.001$). Furthermore, diabetic rats treated with Met plus *E. purpurea* generated asubstantial decrease ($p \leq 0.01$) in the kidney weight relative to the Met treated diabetic rats. In addition, diabetic rats treated with Met plus *E. purpurea* generated a substantial decrease ($p \leq 0.01$) in the kidney index relative to the *E. Purpurea* treated diabetic rats (Table 2).

Table 2 Impact of *E. purpurea,* Met, and their mixture on kidney weight and kidney index evaluated in the diabetic rats.

Groups	Kidney weight (g)	Kidney index
Control	1.62 ± 0.19	0.53± 0.07
Diabetic	2.47 ± 0.32 [a]	1.29 ± 0.27 [a]
Diabetic+ *E. purpurea*	1.94 ± 0.11 [b]	0.80 ± 0.09 [b]
Diabetic+Met	2.09 ± 0.40 [b]	0.74 ± 013 [b]
Diabetic+ *E. purpurea* +Met	1.80 ± 0.19 [b,d]	0.62 ± 0.08 [b,c]

Values are presented as mean ± SD (n=10). Significant difference relative to [a]Control; [b]Diabetic; [c]Diabetic + *E. purpurea*; and [d]Diabetic+Met.

Impact of *E. purpurea*, Met, and their mixture on serum glucose and glycated hemoglobin (HbA1c) evaluated in the diabetic rats

Diabetic rats showed significantly ($p \leq 0.001$) increased serum glucose and HbA1c levels compared to the control rats. Administration of *E. purpurea,* Met, and their mixtureto diabetic rats produced a significant decline in serum glucose and HbA1c concentrations ($p \leq 0.001$) relative to the diabetic rats. Diabetic rats treatment with Met alone and incombination with *E. Purpurea* showed a significant reduction in the serum concentrations of glucose ($p \leq 0.05$) and HbA1c($p \leq 0.01$) relative to the *E. purpurea* treated diabetic rats. There was no significant difference between diabetic rats given Met alone and Met plus *E. purpurea*. Diabetic rats treated with *E. purpurea* +Met achieved nearly normal serum glucose and HbA1c levels (Figure 1).

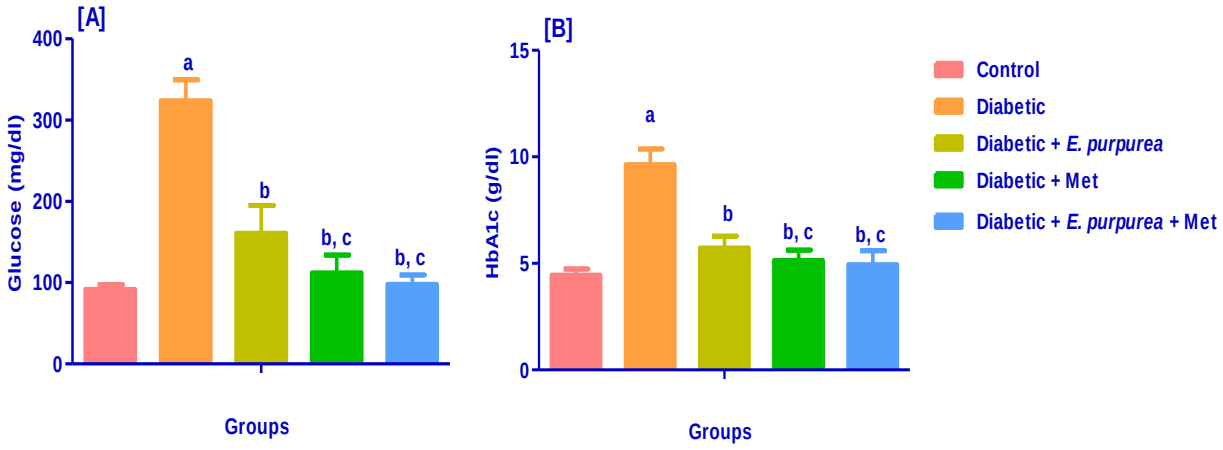

Figure 1 Impact of *E. purpurea*, Met, and their mixture on glucose [A] and HbA1c [B] levels evaluated in the diabetic rats. Values are presented as mean ± SD (n=10). Significant difference relative to [a]Control; [b]Diabetic; and [c]Diabetic + *E. purpurea*.

Impact of *E. purpurea*, Met, and their mixture on serum kidney functions evaluated in the diabetic rats

Diabetic rats showed significantly ($p \leq 0.001$) increased serum blood urea nitrogen and creatinine levels compared to the control rats. Administration of *E. purpurea,* Met, and their mixture to diabetic rats caused a significant decline in serum blood urea nitrogen and creatinine levels relative to the diabetic rats ($p \leq 0.001$). Diabetic rats consumed Met+ *E. Purpurea* showed a significant decrease in the serum levels of blood urea nitrogen and creatinine relative to *E. Purpurea* and Met treated diabetic rats ($p \leq 0.001$). In diabetic groups treated with *E. purpurea* alone and Met alone, there was no substantial difference in serum blood urea nitrogen and creatinine levels. Diabetic rats treated with *E. purpurea* +Met achieved nearly normal serum blood urea nitrogen and creatinine levels (Table 3).

Table 3 Impact of *E. purpurea,* Met, and their mixture on serum kidney functions evaluated in the diabetic rats

Groups	Blood urea nitrogen (mmol/L)	Creatinine(mmol/L)
Control	17.45 ± 2.53	0.66 ± 0.15
Diabetic	42.65 ± 5.09[a]	1.79 ± 0.14[a]
Diabetic+ *E. purpurea*	29.55 ± 3.97[b]	1.05 ± 0.19[b]
Diabetic+Met	28.05 ± 3.59[b]	1.08 ± 0.20[b]
Diabetic+ *E. purpurea* +Met	19.74 ± 4.20[b,c,d]	0.79 ± 0.10[b,c,d]

Values are presented as mean ± SD (n=10). Significant difference relative to [a]Control; [b]Diabetic; [c]Diabetic + *E. purpurea*; and [d]Diabetic +Met.

Impact of *E. purpurea*, Met, and their mixture on serum pro-inflammatory cytokines evaluated in the diabetic rats

Diabetic rats showed a substantial increase in serum pro-inflammatory cytokines levels (IL-1β and IL-6) compared to the control rats ($p \leq 0.001$). Administration of *E. purpurea,* Met, and their mixture to diabetic rats produced asignificant reduction in the serum IL-1β and IL-6 levels compared to the diabetic rats ($p \leq 0.001$). Treatment of diabetic rats with *E. purpurea*+Met produced a significant decrease in IL-1β and IL-6 levels compared to *E. Purpurea* ($p \leq 0.05$) and Met ($p \leq 0.001$) rats. There was a significant difference ($p \leq 0.01$) between diabetic rats consuming Met and diabetic rats consuming *E. purpurea* in IL-1β and IL-6 levels (Figure 2).

Impact of *E. purpurea*, Met, and their mixture on kidney oxidative stress indices evaluated in diabetic rats

Diabetic rats exhibited a substantial reduction in renal SOD concentration and a substantial rise in renal MDA content relative to the control rats ($p \leq 0.001$). Consumption of *E. purpurea,* Met, and their mixture to diabetic rats produceda substantial rise in renal SOD activity and a substantial reduction in renal MDA content relative to the diabetic rats ($p \leq 0.001$). Diabetic rats treated with *E. purpurea*+Met produced significant differences in renal SOD and MDA contents compared to the diabetic rats treated with *E.*

Purpurea (p≤ 0.01) and Met (p≤ 0.001). There was a significant (p ≤ 0.01) difference between diabetic rats consuming Met and diabetic rats cosuming *E. Purpurea* concerning renal SOD and MDA content (Figure 3).

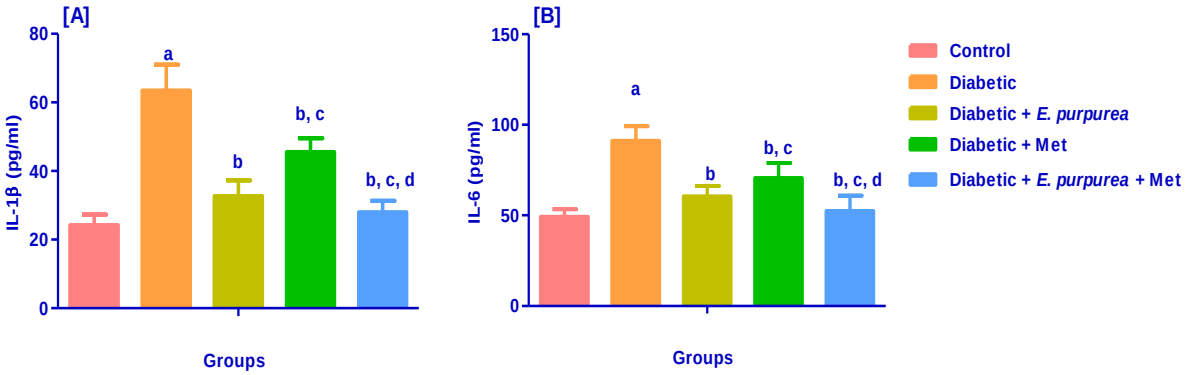

Figure 2 Impact of *E. purpurea*, Met and their mixture on serum IL-1β [A] and IL-6[B] levels evaluated in the diabetic rats. Values are presented as mean ± SD (n=10). Significant difference relative to [a]Control; [b]Diabetic; [c]Diabetic + *E. purpurea*; and [d]Diabetic +Met.

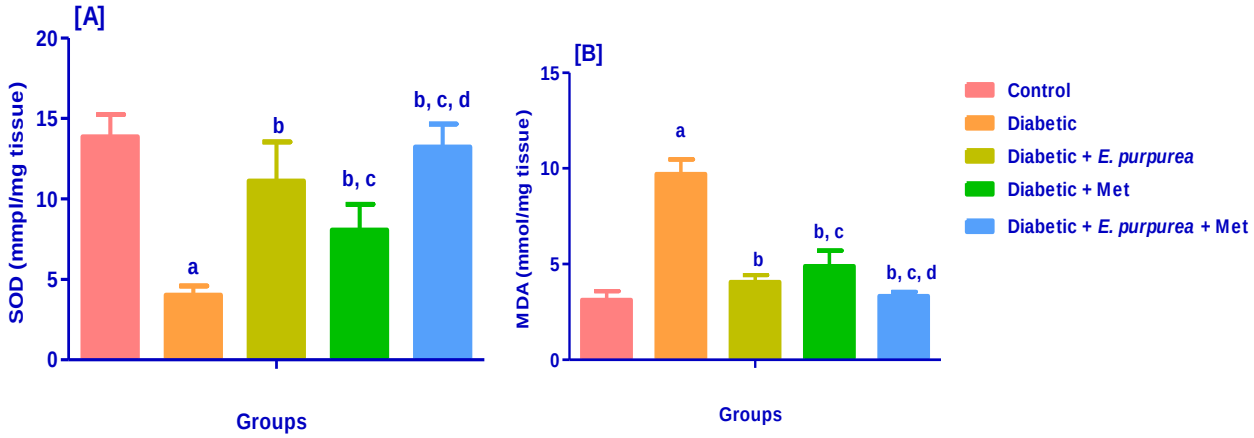

Figure 3 Impact of *E. purpurea*, Met, and their mixture on kidney oxidative stress indices SOD [A] and MDA [B] levels evaluated in diabetic rats. Values are presented as mean ± SD (n=10). Significant difference relative to [a]Control; [b]Diabetic; [c]Diabetic + *E. purpurea*; and [d]Diabetic +Met.

Histopathological examination

Microscopically, kidney sections of control rats presented with normal structure of renal tubules, parenchyma, and glomeruli (Figure 4 A and Figure 5 A). kidney sections of diabetic rats presented with severe histopathological alteration, including interstitial nephritis, cystic dilatation of renal tubules, periglomerular inflammatory cells infiltration, and thickening and dilatation of the parietal layer of Bowman's capsule (Figure 4 B and Figure 5 B). Kidney sections of diabetic rats treated with *E. purpurea* showed mild interstitial nephritis, few inflammatory cell infiltration, and congestion of glomerular tuft (Figure 4C and Figure 5C). Similarly, kidney sections of diabetic rats treated with Met showed mild interstitial nephritis and eosinophilic renal cast in the tubules' lumen (Figure 4D and Figure 5D). Conversly, kidney sections of diabetic rats consumed the mixture of *E. Purpurea* and Met showed nearly normal kidney histology with only slight glomerular tuft congestion (Figure 4E and Figure 5E).

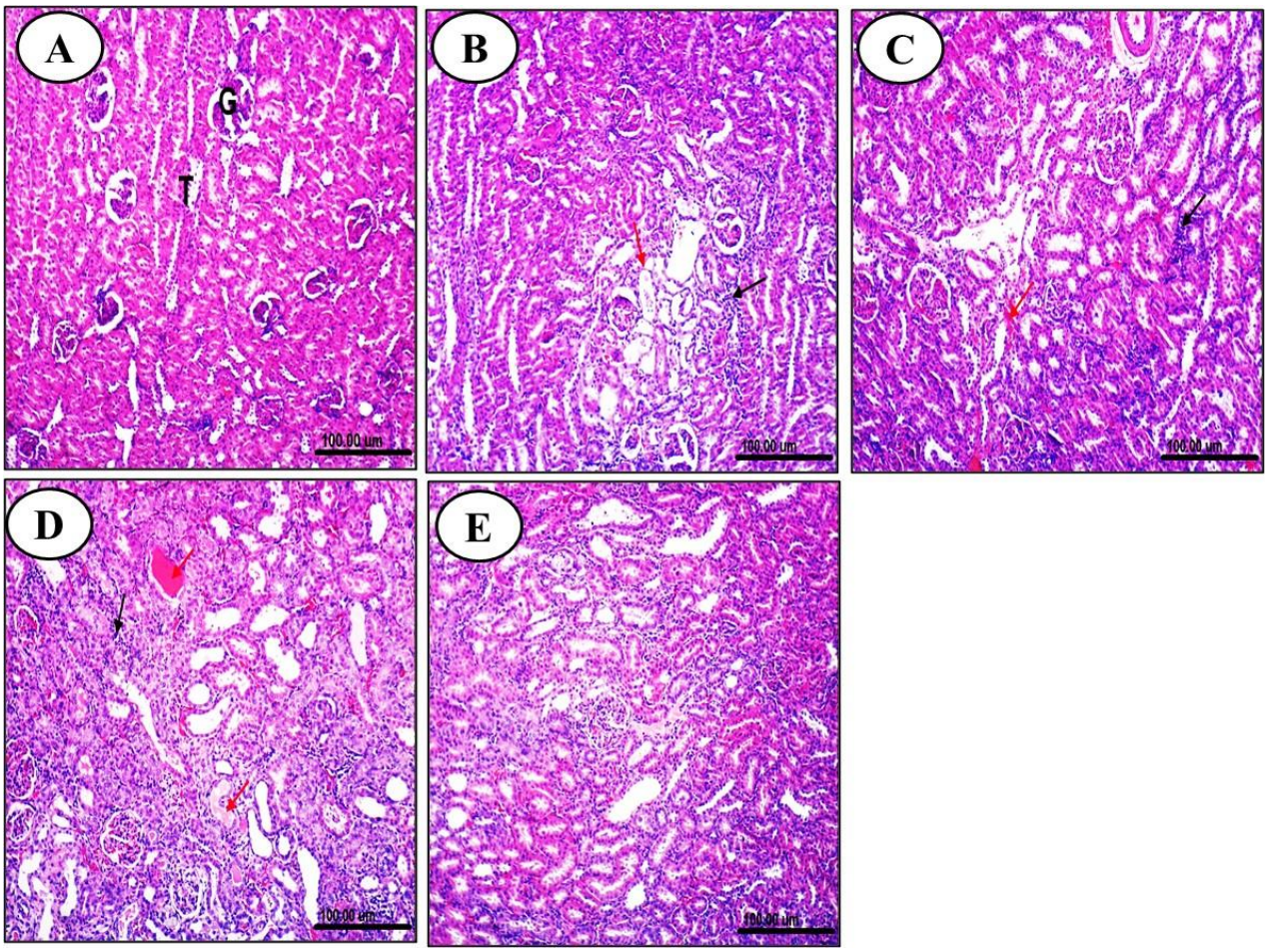

Figure 4 Impact of *E. purpurea,* Met, and their mixture on renal histopathology evaluated in the diabetic rats (H & E X 100, scale bar 100um). Photo A represents the control group: Displayed healthy histological structure of renal parenchyma, glomeruli (G), and renal tubules (T). Photo B represents the diabetic group: Displayed interstitial nephritis (black arrow) and cystic dilatation of renal tubules (red arrow). Photo C represents the diabetic + *E. purpurea* group: Displayed mild interstitial nephritis (black arrow) and congestion of renal blood vessel (red arrow). Photo D represents the diabetic + Met group: Displayed interstitial nephritis (black arrow) and eosinophilic renal cast in the renal lumen tubules (red arrow). Photo E represents the diabetic + *E. purpurea* + Met group: Displayed nearly normal histology.

4. DİSCUSSİON

Several DIAB-related metabolites, including glucose, are linked to the etiology of DN. The disease's etiology is influenced by inflammation, oxidative stress, and other causes. Increased blood glucose concentration is the first and most important factor in people with DIAB (Giacco and Brownlee, 2010; Mao et al., 2018). In the present study, DN was confirmed in the diabetic rats by fasting hyperglycemia and increased HbA1c, high serum blood urea nitrogen and creatinine levels, and severe pathological alteration in kidneys, including interstitial nephritis, cystic dilatation of renal tubules, periglomerular inflammatory cells infiltration, and thickening and dilatation of the parietal layer of Bowman's capsule, and the increase in kidney weight. However, accelerated muscle loss and peripheral lipolysis because of the decline in insulin secretion may also clarify the DIAB rats' accompanying decreased body weight in this research (Enoksson et al., 2003). These findings are consistent with several preceding studies that have found comparable findings in the same experimental model (Pourghasem et al., 2015; Qiao et al., 2017; ALTamimi et al., 2021).

In diabetic rats, *E. purpurea* alone and in combination with Met significantly reduced serum glucose and HbA1c compared to diabetic rats. However, it was discovered that combining *E. purpurea* with Met resulted in better glucose regulation than *E. purpurea* alone. The combined therapy maintains the normal range's glucose level (70-110mg/dl). These findings contradicted Mao's findings, which showed that the blood glucose level of diabetic rats treated with nano *E. Purpurea* remained elevated at 120 minutes of the glucose tolerance test compared to diabetic rats. However, their findings support ours in terms of the nano *E. Purpurea*'s antihyperglycemic behavior when combined with Met (Mao et al., 2018). According to early studies, *E. purpurea* can help managetype 2DIAB (Christensen et al., 2009; Kotowska et al., 2014). Alkamide and fatty acid, two active constituents of *E. purpurea* flowers, were found to activate peroxisome proliferator-activated receptors (PPARs)-gamma proteins, resulting in improved insulin

sensitivity allowing cells to absorb more glucose (Christensen et al., 2009). In addition, PPAR-gamma proteins were also enabled by crude extracts of *E. purpurea* roots, which improved glucose absorption in cells. Researchers were able to separate the molecules from the crude extract and discovered that the bioactive components were alkamides in the roots (Kotowska et al., 2014). Consequently, these will increase cell energy and reduces the elevated blood sugar levels in diabetic patients. Furthermore, *Echinacea* can be less dangerous than oral hypoglycemic agents, which frequently have harmful side effects. Many professionals recommend against consuming *Echinacea* if you have type 1 DIAB. This is because this form of DIAB is an autoimmune disorder. Echinacea has been linked to adverse side effects on some minimal occasions regarding people with other autoimmune conditions. Nevertheless, new research indicates that *Echinacea* may help many people suffering from autoimmune diseases like type 1 DIAB. The defective and/or impaired natural killer (NK) immune cells are thought to be the primary trigger of type 1 DIAB. According to a review, oral doses of *echinacea* root substantially increased NK cells' number in an in vivo model of human type 1DIAB, with no adverse consequences. *Echinacea's* capability to boost NK cells has been confirmed in many other experimental models (Miller 2005; Sarubin-Fragakis and Thomson, 2007). According to a recent report, the roots of *E. purpurea* may be responsible for the hypoglycemic behavior observed (Aarland et al., 2017).

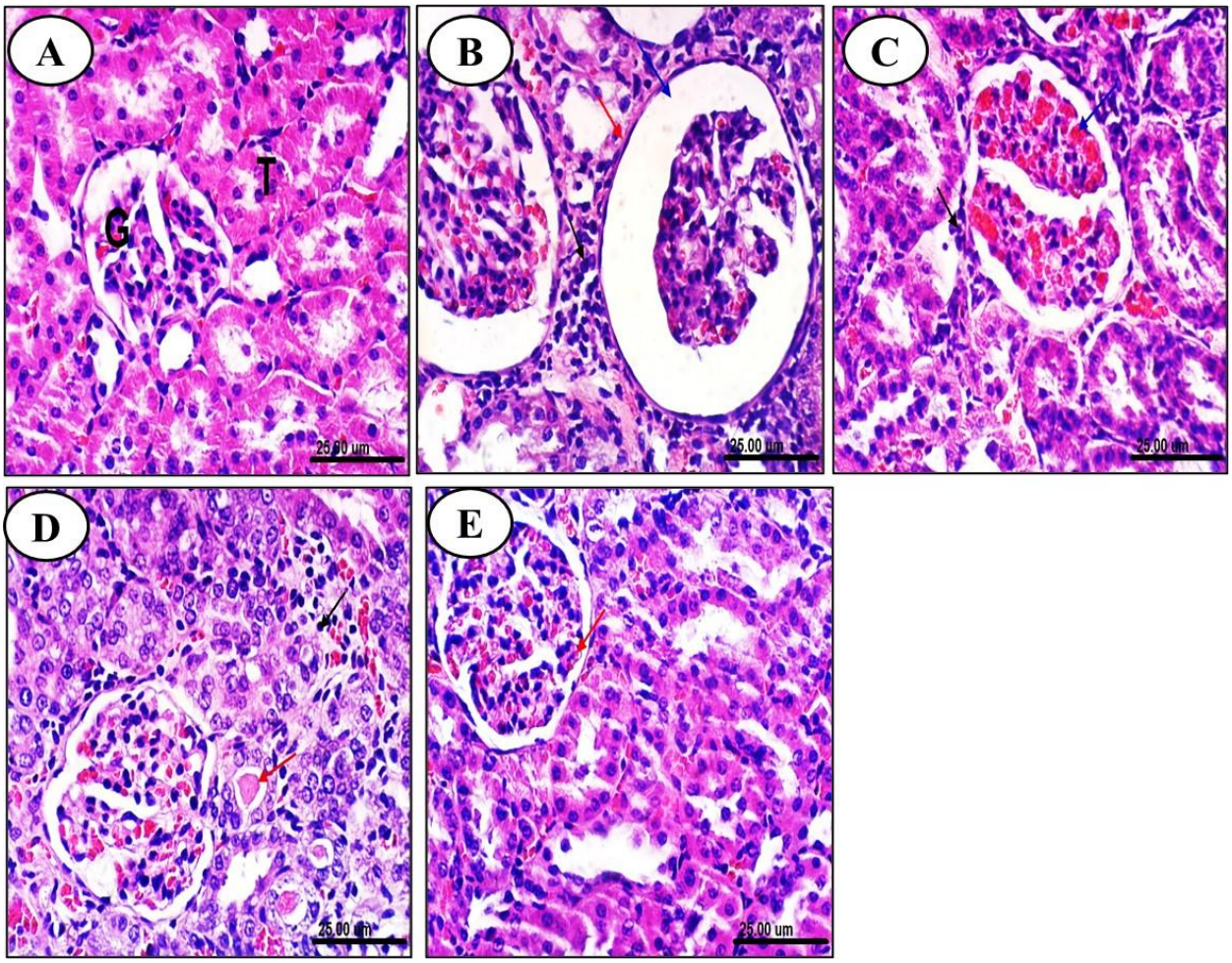

Figure 5 Impact of *E. purpurea,* Met, and their mixture on kidney histopathology evaluated in diabetic rats (H & E X 400, scale bar 25 um). Photo A represents the control group: Displayed healthy histological structure of renal parenchyma, glomeruli (G), and renal tubules (T). Photo B represents the diabetic group: Displayed periglomerular inflammatory cell infiltration (black arrow), thickening of the parietal layer of Bowman's capsule (red arrow), and dilatation of Bowman's space (blue arrow). Photo C represents the diabetic + *E. purpurea* group: Displayed few inflammatory cell infiltration (black arrow) and congestion of glomerular tuft (blue arrow). Photo D represents the diabetic +Met group: Displayed interstitial nephritis (black arrow) and eosinophilic renal cast in the renal lumen tubules (red arrow). Photo E represents the diabetic + *E. purpurea* +Met group: Displayed apparently normal kidney histology, with slight congestion of glomerular tuft (red arrow).

This study's findings showed that *E. purpurea*, alone or combined with Met, significantly reduced DN in diabetic rats. Hypoglycemic effects, antioxidants, and anti-inflammatory effects were discovered to be protective mechanisms. The results also suggested that *E. purpurea* in combination with Met may be a more effective DN inhibitor. To the best of our knowledge, no

research has been done on the impact of *E. Purpurea* root extract on DIAB-related kidney injury. However, *E. purpurea*'s protective effect against kidney damage caused by the famous cancer treatment drug cisplatin has recently been discovered (Turkistani, 2019). In line with the findings of the current study, Turkistani indicated that the *E. Purpurea* root extract improved kidney function by lowering serum levels of creatinine and blood urea nitrogen and improving kidney tissue structure compared to the cisplatin group (Turkistani, 2019). This research found that *E. Purpurea* root extract decreased MDA level (lipid peroxidation product) and increased the level of the SOD (antioxidant enzyme). Turkistani also agreed with our findings, reporting that the *E. Purpurea* root extract reduced thiobarbituric acid reactive substances (lipid peroxidation products) and increased the level of catalase (CAT) and the glutathione peroxidase (GPx) (antioxidant enzymes) (Turkistani, 2019).

Furthermore, the present results observed that *E. Purpurea* root extract decreased IL-1β and IL-6 levels (pro-inflammatory cytokines). In line with these results, Turkistani showed that *E. purpurea*root extract reduced TNF-α (a pro-inflammatory cytokine) (Turkistani, 2019). Several studies have been previously conducted that confirmed *E. Purpurea* root extract anti-inflammatory and antioxidant properties (Pellati et al., 2005; Huntimer et al., 2006; Ali 2008; Sullivan et al., 2008; Aarland et al., 2017; Coelho et al., 2020). The fundamental behind *E. Purpurea* root extract's renoprotective effect seems to be the recovery of antioxidants and the suppression of inflammation.The *E. Purpurea* root extract's most active constituents are polysaccharides, phenolic acids, alkylamides, phenolic diterpenes, polyacetylene, glycoproteins, tannins, inulin, flavonoids, and isohytylamides (Goel et al., 2005, Turkistani, 2019). Polysaccharides and alkamides of *E. Purpurea* root extract have been shown to have anti-inflammatory and immunomodulatory properties (Manayi et al., 2015). Moreover, *E. purpurea* root extract polyphenols improved kidney damage and increased antioxidant status in kidney tubules (Rezaie et al., 2013). Cichoric acid in *E. purpurea* root extract has also been shown to have anti-free radical properties (Manayi et al., 2015). In rats with ischemia/reperfusion injury, (Bayramoglu et al., 2011) discovered that *E. purpurea* root extracts reduced liver and kidney damage. Furthermore, *E. purpurea* extract reduced gentamicin-induced renal toxicity and protected against its adverse effects on kidney function (Angouti and Mashayekhi, 2017).

5. CONCLUSİON

This study showed a protective effect of *E. purpurea* root extract against the kidney damage associated with DIAB induced by STZ in rats. This is clearly demonstrated by the improvement in kidney function and pathology. This improvement may be due to the extract's hypoglycemic, antioxidant, and anti-inflammatory effects.

Authors' contributions: This work was carried out in collaboration among all authors.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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